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AMENDMENT TO THE SPECIFICATION

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims:

1. (Currently Amended) A substantially pure nucleic acid molecule having at least 90% sequence identity to SEQ ID NO: 1 and encoding a mammalian methionine synthase reductase polypeptide, wherein said polypeptide is capable of catalyzing the reductive methylation of methionine synthase-cob(II)alamin to generate methionine synthase-cob(III)alamin-CH3.

2. (Currently Amended) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule encodes a human polypeptide.

3. (Currently Amended) The nucleic acid of claim 1, wherein said nucleic acid molecule has the sequence of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, or degenerate variants thereof, and wherein said nucleic acid molecule encodes the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 46, or SEQ ID NO: 48, respectively.

4. (Currently Amended) A substantially pure nucleic acid molecule that hybridizes in 2X SSC medium at 40°C to the polynucleotides of ~~a sequence found within~~ SEQ ID NO: 1, ~~or~~ SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, wherein the administration of

said nucleic acid molecule to a subject leads to a decrease in the expression of methionine synthase reductase polypeptide in said subject, relative to a control subject not administered said nucleic acid molecule ~~wherein said nucleic acid comprises a region complementary to a naturally occurring mammalian methionine synthase reductase mutation or polymorphism~~.

5. (Currently Amended) The nucleic acid molecule of claim 4, wherein said nucleic acid molecule has a sequence completely complementary to at least 30 ~~50% of at least 60~~ contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47 ~~or SEQ ID NO: 41~~. NO function

35. (Cancelled)

36. (Currently Amended) A substantially pure nucleic acid molecule having a polynucleotide sequence that has at least 50% sequence identity to SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47 over the entire length of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, respectively, wherein said nucleic acid molecule encodes a polypeptide capable of catalyzing the reductive methylation of enzymatically inactive methionine synthase-cob(II)alamin to generate enzymatically active methionine synthase-cob(III)alamin-CH3.

37. (Currently Amended) The nucleic acid molecule of claim 36, wherein said ~~having a~~ polynucleotide sequence ~~that~~ has at least 85% sequence identity to SEQ ID NO: 1, SEQ ID NO:

41, SEQ ID NO:43, SEQ ID NO: 45, or SEQ ID NO: 47 over the entire length of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, respectively.

38. (Currently Amended) The nucleic acid molecule of claim 37, wherein said ~~having a~~ polynucleotide sequence ~~that~~ has at least 95% sequence identity to SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47 over the entire length of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, respectively.

OK

39-40. (Cancelled)

41. (Currently Amended) A substantially pure nucleic acid molecule having a polynucleotide sequence that has at least 50% sequence identity to a sequence that is complementary to ~~the corresponding region of~~ SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, wherein the administration of said nucleic acid molecule to a subject leads to a decrease in the expression of methionine synthase reductase polypeptide in said subject, relative to a control subject not administered said nucleic acid molecule ~~, wherein said nucleic acid comprises a naturally-occurring mammalian methionine synthase reductase mutation or polymorphism~~.

Completely no function WD SE

42. (Currently Amended) The nucleic acid molecule of claim 41, wherein said polynucleotide sequence ~~having a polynucleotide sequence that~~ has at least 85% sequence identity to a sequence that is complementary to ~~the corresponding region of~~ SEQ ID NO: 1, SEQ

WD/SE no function

Completely

ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

43. (Currently Amended) The nucleic acid molecule of claim 42, wherein said polynucleotide sequence ~~having a polynucleotide sequence that~~ has at least 95% sequence identity to a sequence that is complementary to ~~the corresponding region of~~ SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

44. (Cancelled)

45. (Currently Amended) The nucleic acid molecule of claim 1 or 36 ~~1, 36, or 41~~, wherein said nucleic acid molecule encodes ~~encoding~~ a mammalian methionine synthase reductase polypeptide having at least 20 to 30% ~~20-30%~~ of the biological activity of ~~ability to catalyze the reductive methylation of methionine synthase cob(II)alamin to generate methionine synthase cob(III)alamin-CH3 as~~ the methionine synthase reductase polypeptide of SEQ ID NO: 2.

46. (Currently Amended) The nucleic acid molecule of claim 45, wherein said nucleic acid molecule encodes ~~encoding~~ a mammalian methionine synthase reductase polypeptide having at least 55 to 75% ~~55-75%~~ of the biological activity of ~~ability to catalyze the reductive methylation of methionine synthase cob(II)alamin to generate methionine synthase cob(III)alamin-CH3 as~~ the methionine synthase reductase polypeptide of SEQ ID NO: 2.

47. (Currently Amended) The nucleic acid molecule of claim 1 or 36 ~~1, 36, or 41~~, wherein said nucleic acid molecule encodes ~~encoding~~ a mammalian methionine synthase reductase polypeptide that comprises a consensus binding site for one or more cofactors selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises any one of SEQ ID NOs: 25-40.

48. (Withdrawn) The nucleic acid of claim 47, wherein said binding site comprises a sequence that is at least 70% identical to one of the following sequences:

(a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),

(b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),

(c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),

(d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),

(e) FVFNIVEFLSTATT (SEQ ID NO: 56),

(f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),

(g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),

(h) SFSRDA (SEQ ID NO: 59),

(i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV

(SEQ ID NO: 60), or

(j) KRYLQDIWS (SEQ ID NO: 61).

49. (Withdrawn) The nucleic acid of claim 48, wherein said binding site comprises a sequence that is identical to one of the following sequences:

(a) FLLLYATQQGQAKAIAEEMC (SEQ ID NO: 52),

(b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),

(c) AHLRYGLLGLGDSEYTYFCNGGKIIDKRL (SEQ ID NO: 54),

(d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),

(e) FVFNIVEFLSTATT (SEQ ID NO: 56),

(f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),

(g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),

(h) SFSRDA (SEQ ID NO: 59),

(i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV

(SEQ ID NO: 60), or

(j) KRYLQDIWS (SEQ ID NO: 61).

50-51. (Cancelled)

WD/SE

52. (Currently Amended) The nucleic acid molecule of claim 4 or 41 ~~51~~, wherein said ~~the administration of said nucleic leads to a decrease in the activity of said mutant~~ methionine synthase reductase polypeptide is a mutant or polymorphic methionine synthase reductase polypeptide.

NO function

WD/SE

53. (Currently Amended) The nucleic acid molecule of claim 4 ~~or 41~~, wherein said nucleic acid molecule comprises a polynucleotide sequence the complement of which comprises a ~~said~~ naturally-occurring mammalian methionine synthase reductase mutation or polymorphism.

54. (New) The nucleic acid molecule of claim 36, 37, or 38, wherein said polynucleotide sequence comprises a naturally-occurring mammalian methionine synthase reductase mutation or polymorphism.

55. (New) The nucleic acid molecule of claim 41, 42, or 43, wherein the complement of said polynucleotide sequence comprises a naturally-occurring mammalian methionine synthase reductase mutation or polymorphism.